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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,701	01/14/2002	Klaus Ducker	MERCK 2354	8622

23599 7590 10/18/2004

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,701	DUCKER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 12-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 12-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-19 are pending. Claims 10-11 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-9, 12-19 are under consideration.

Response to Amendment and Arguments

Applicant's amendment and arguments filed 8/17/2004 have been fully considered but they are persuasive in part.

The Objections to the Title and Specification have been obviated by Applicant's amendment and are thus withdrawn.

The rejection of claims 1, 4-8 under 35 USC § 112 first paragraph as being indefinite for the recitation of the term "stringent conditions" has been obviated by Applicant's amendment is thus withdrawn.

Remaining issues are set forth below.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 stand rejected, and new claims 12-19 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth in the office action of 05/17/2004. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The rejection of record set forth that it is clear from the instant specification that the nucleic acid encoding the ICSR-1 polypeptide has been assigned a function because of its similarity to known proteins (Specification at 8). However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors. Further, the rejection set forth that even if, *arguendo*, the nucleic acid encoding the ICSR-1 protein is found to be a GPCR, the ligand is unknown. Since the ligand of this protein is unknown, the function of the protein is also unknown. Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the ICSR-1 protein, therefore, there is no "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. The previous office action set forth that after complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant claims are drawn to a nucleic acid

encoding a polypeptide, which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as ICSR-1, the instant invention is incomplete. The polypeptide encoded by the nucleic acids of the instant invention is known to be structurally analogous to proteins that are known in the art as GPCRs. In the absence of knowledge of the natural ligand or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances that inhibit its activity is clearly to use it as the object of further research that has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for ICSR-1 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

According to MPEP § 2107, a rejection for lack of utility is imposed when an invention lacks an asserted specific and substantial utility and it does not have a readily apparent well-established utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

Applicant argues that the claimed polynucleotides and polypeptides can be used as markers for heart tissue, and points to Example 8 (on Page 33 of the specification), which discloses the highly specific expression of ICSR-1 in cardiac tissues. See, Fig 1A. Applicant further argues that the gene is expressed at very high levels in ventricle tissue, but substantially

absent from auricle tissue. Applicant argues that the nucleic acid can be used as a unique and tissue-specific marker for ventricle tissues. (See page 15, lines 23-27).

However, the nucleic acid and encoded protein lacks an asserted specific and substantial utility because while the Specification asserts that the polynucleotide sequences are valuable tools for tissue expression studies (page 15, lines 23-35), and that such studies allow the determination of expression patterns of the instant polynucleotides, the Specification does not disclose information regarding the nexus between ICSR-1 expression or function and a pathological condition, thus this asserted utility is neither specific nor substantial. Significant further experimentation would be required of the skilled artisan to determine whether ICSR-1 expression or function was involved in a pathological condition, and to identify individuals with such a disease. There must be some expression pattern that would allow the claimed polynucleotide or polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide or polypeptide is expressed in higher levels in the diseased state compared to normal expression (i.e. overexpression). Applicant further argues that tissue-specificity was published by the Patent Office as sufficient to meet the statutory requirements of § 101, and cites Example 12 of the Revised Interim Utility Guidelines Training Materials which is of a marker that is specific for a cancer - which is a type of tissue specificity. Applicant argues that there is no reason why tissue specificity of normal tissue (e.g., for cardiac tissues) would not analogously satisfy the utility requirements. However, in contradistinction to Example 12 of the Utility Guidelines, the nexus between ICSR-1 expression or function and a pathological condition are not disclosed. Evidence of a differential expression might serve as a basis for use of the claimed

polynucleotide or polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or polypeptide and any disease or disorder and the lack of any correlation between the claimed polynucleotide or polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself.

Applicant further argues that since the Written Description Guidelines provide an Example wherein a polypeptide is used as a marker for normal tissue the ICSR-1 polynucleotide and polypeptide should meet the utility requirement. However, the Written Description Guidelines are silent with regard to issues arising under 35 USC § 101.

Claims 1-9 stand rejected, and new claims 12-19 are also rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the Office Action of 05/17/2004. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The rejection of record set forth that even if, *arguendo*, the nucleic acid of the instant invention is found to have a patentable utility, claims 1-9 stand rejected, and new claims 12-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 2, or a nucleic acid with the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for a nucleic acid which is 95% identical to SEQ ID NO: 1; or a polypeptide 95% identical to SEQ ID NO: 2; or variants and fragments of SEQ ID NO: 1; or fragments of SEQ ID NO: 1 having at least 20 or 50 nucleotides; or fragments and variants of SEQ ID NO: 2; or host cells comprising such

polynucleotides; or fusion proteins comprising such polypeptides; or polypeptides comprising at least 5, 10 or 30 amino acids of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record set forth that Claims 1-9 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of ICSR-1. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of ICSR-1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell.

Applicant argues that methods of hybridization can be used to isolate sequences which hybridize under stringency conditions to the sequence set forth in SEQ ID NO: 1, see, e.g. page 10, lines 1-14, and that given this disclosure and the mature state of the art it is evident that the skilled worker at the time the application was filed could routinely determine other polynucleotides and polypeptides encoded thereby which fall within the scope of the claims. Moreover, Applicant argues, that they could be tested for activity and tissue-specific activity as described on Pages 30-33 of the specification. However, the Specification only shows that the full-length nucleic acid of SEQ ID NO: 1 will serve as a marker for ventricular tissue, while the claims encompass variant nucleic acids and polypeptides. The Specification does not disclose the critical nucleic acid residues necessary to maintain the function of detecting ventricular

tissue. The specification does not disclose the correlation between the structure (sequence) of the encompassed nucleic acids and the function of detecting ventricular tissue. The nucleic acid sequence determines its structural and functional properties, and predictability of which nucleic acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the nucleic acids are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Therefore it would require undue experimentation by one of skill in the art to make and use the invention as claimed without further guidance from the instant specification.

Claims 1-9 stand rejected and new claims 12-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 5/17/2004. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a nucleic acid which is 95% identical to SEQ ID NO: 1; or a polypeptide 95% identical to SEQ ID NO: 2; or variants and fragments of SEQ ID NO: 1; or fragments of SEQ ID NO: 1 having at

least 15 or 100 nucleotides; or fragments and variants of SEQ ID NO: 2; or host cells comprising such polynucleotides; or fusion proteins comprising such polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 1 and the polypeptide of SEQ ID NO: 2 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the Specification provides clear guidance on how to isolate polynucleotides and polypeptides that fall within the scope of the claims. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show

the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as functional characteristics coupled with a known or disclosed correlation between structure and function of the claimed genus of polynucleotides or polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed which have the claimed function. Thus, no identifying characteristics or properties of the instant polynucleotides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID NO: 1 or 2 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 12-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "specific" in claims 1 and 4 is a relative term that renders the claims indefinite. The term "specific" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claims 2-3, 5-9, 12-19 are rejected insofar as they depend on the recitation of the term " specific ".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-8 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,759,804 (Godiska et al.), for reasons of record set forth in the Office Action of 5/17/2004.

The rejection of record set forth that the '804 patent disclose the cloning and expression of several G protein coupled receptors (column 3, lines 15-30). The nucleic acid sequence which encodes the R12 GPCR is set forth in SEQ ID NO: 43, and is 11.7% identical to the instant sequence of SEQ ID NO: 1, (see Sequence Comparison A, attached). This nucleic acid anticipates claims 4-5 because it comprises sequences which are "fragments or variants" of SEQ ID NO: 1, and also contains a stretch of 15 nucleic acids which is 100% identical to SEQ ID NO: 1. Claims 6-8 are anticipated because the '804 patent discloses expression vectors and host cells comprising the polynucleotides (column 3, lines 43-65) as well as method of producing the encoded protein (column 4, lines 1-15). The '804 patent also discloses that amino acid sequence of the encoded R12 polypeptide in SEQ ID NO: 44, which is 19.7% identical to instantly claimed

SEQ ID NO: 2 (see Sequence Comparison B, attached). Claim 1 is anticipated because the R12 polypeptide comprises sequences that are fragments or variants of SEQ ID NO: 2.

Applicant has added the limitation wherein the fragments are "specific" fragments, however, there is no structural information provided as to what is a specific fragment, such as the length of the fragment. Additionally, there is no metric by which to determine whether the fragment is specific (see rejection under 35 USC § 112 second paragraph, supra). Thus since there is no structural limitation regarding the fragment, nor is there another way to determine the specificity of the fragment, the claims are anticipated.

Conclusion

Claims 1-9, 12-19 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

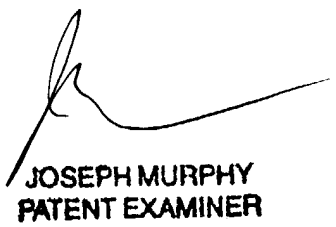
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
October 13, 2004